

REMARKS

Claims 34 and 38 have been amended to correct in advertent typographical errors. No new matter has been added by the amendments.

Claims 18-38 are pending in the application, with claims 18 and 34 being the independent claims. Claims 34 and 38 have been withdrawn from consideration by the Examiner.

I. Statement of Substance of the Interview

Applicants thank Examiners Liu and Wyrozewski for the person interview conducted on May 13, 2010, with Applicants' undersigned representative. During the interview, the differences between ultrasonic atomization of Bittner and ultrasonic nebulization, as recited in the claims, were discussed. It was agreed that Zimmerman in view of Bittner does not teach the claimed invention since Bittner discloses an ultrasonic atomization method, which is distinct from the ultrasonic nebulization of the presently claimed invention.

II. The Rejection of Claims 18-19 and 21-27 Under 35 U.S.C. § 103(a) Should be Withdrawn

Claims 18-19 and 21-27 have been rejected at pages 3-5 of the Office Action as allegedly being unpatentable over Zimmermann, U.S. Patent No. 6,465,226 (hereinafter "Zimmermann") in view of Bittner *et al.*, *J. Microencapsulation* 16:325-341 (1999) (hereinafter "Bittner"). Applicants respectfully traverse this rejection.

The Office Action suggests that Zimmermann discloses a process for preparing microspheres comprising an ionically crosslinked polymer, the process comprising producing liquid droplets from a solution comprising an ionically crosslinkable polymer into a gas stream using a nebulizing nozzle, and transferring the gas stream into a gelling solution.

The Office Action concedes that Zimmermann does not teach using an ultrasonic nebulizer to form the gas stream. The Office Action attempts to cure this deficiency with the disclosure of Bittner, asserting that Bittner discloses an ultrasonic atomization method for preparing microspheres. The Office Action also indicates that Zimmermann does not explicitly disclose separating the microspheres from the gelling solution. However, the Office Action

suggests that it is inherent that the microspheres are separated from the gelling solution in Zimmermann.

The Office Action contends that:

[i]t would have been obvious to one of ordinary skill in the art at the time of the invention to provide the ultrasonic nebulizer as taught by Bittner et al. in the process of Zimmermann since Bittner et al. teach that ultrasonic nozzles have the advantage of generating droplets with a relatively uniform size distribution which could lead to more homogeneous size distribution of microspheres.

Office Action at page 4, fourth paragraph (citations omitted). The Office Action therefore concludes that the claimed invention would have been obvious. Applicants respectfully disagree with these contentions and conclusions.

The Office Action states, “Zimmermann does not teach using an ultrasonic nebulizer for forming the continuous gas stream. However, Bittner et al. teach an ultrasonic atomization method for preparing microspheres by using an ultrasonic atomizer” Office Action at page 4, lines 4-7.

Applicants respectfully submit, as stated in the Office Action, Bittner discloses *ultrasonic atomization using an ultrasonic atomizer*. Bittner does not disclose producing liquid aerosol droplets from a solution comprising an ionically crosslinkable polyionic polymer into a continuous gas stream *by using an ultrasonic nebulizer*, as recited in the presently claimed invention.

A person of ordinary skill in the art would understand that the process of producing liquid droplets using an *ultrasonic atomizer* disclosed in Bittner is clearly distinct from the process of the presently claimed invention that uses an *ultrasonic nebulizer*. As stated in Bittner, “[t]he generation of biodegradable microspheres using ultrasonic atomization in conventional laboratory *spray drying equipment* is reported here.” Bittner at page 326, last paragraph (emphasis added). Ultrasonic atomization requires passing air across an opening to draw liquid from a storage receptacle, which this then atomized into liquid droplets. *See id.* at page 327, Figure 1, elements 6 and 7.

In contrast, the ultrasonic nebulizer utilized in the presently claimed invention uses an ultrasound generator situated in a nebulizing chamber filled with a solution comprising an ionically crosslinkable polyionic polymer to nebulize liquid aerosol droplets from the solution

into a continuous gas stream. See Present Specification at page 4 and Figure 1. Applicants respectfully submit that the atomic atomizer disclosed in Bittner is not the same, and does not function in the same way, as the ultrasonic nebulizer utilized in the practice of the presently claimed invention.

As set forth in the Interview Summary dated May 14, 2010, during the personal interview with Examiner's Liu and Wyrozebski, it was agreed that Zimmerman in view of Bittner does not teach the claimed invention since Bittner discloses an ultrasonic atomization method, which is distinct from the ultrasonic nebulization of the presently claimed invention.

Even assuming that Bittner could be properly combined with the disclosure of Zimmermann, which it cannot as explained in Applicants' Reply to Office Action filed on July 1, 2009 (the disclosure of which is incorporated by reference herein in its entirety), this combination does not render obvious the presently claimed processes. Thus, as Zimmermann and Bittner do not disclose the presently claimed invention alone or in combination, the Office Action has not set forth a proper *prima facie* case of obviousness. See M.P.E.P. § 2143.03.

In view of the foregoing remarks, Applicants respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. § 103(a).

III. The Rejection of Claims 20 and 28 Under 35 U.S.C. § 103(a) Should be Withdrawn

Claims 20 and 28 have been rejected at pages 5-6 of the Office Action as allegedly being unpatentable over Zimmermann in view of Bittner and further in view of Lim, U.S. Patent No. 4,352,883 (hereinafter "Lim"). Applicants respectfully traverse this rejection.

The Office Action suggests that the combined disclosures of Zimmermann and Bittner disclose the claimed invention as set forth above. The Office Action, however, indicates that these references do not disclose that the polyvalent cation of the gelling solution is selected from the compositions set forth in present claim 20, or that the metal cation is Ca^{2+} , as set forth in present claim 28. The Office Action attempts to cure these deficiencies with the disclosure of Lim, suggesting that Lim discloses the polyvalent cation polyethyleneimine of a gelling solution and the use of Ca^{2+} as the metal cation of a gelling solution. The Office Action therefore concludes that the claimed invention would have been obvious. Applicants respectfully disagree with these contentions and conclusions.

As set forth above, Applicants submit that Zimmermann and Bittner, alone or in combination, fail to disclose a process for preparing microspheres using an ultrasonic nebulizer, as recited in the presently claimed invention. Lim also fails to cure these deficiencies. Thus, Zimmermann, Bittner and Lim, alone or in combination, do not disclose the presently claimed invention.

In view of the foregoing remarks, Applicants respectfully submit that the Office Action has failed to set forth a proper *prima facie* case of obviousness. Reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a) are respectfully requested.

IV. The Rejection of Claims 29-30, 32 and 35-37 Under 35 U.S.C. § 103(a) Should be Withdrawn

Claims 29-30, 32 and 35-37 have been rejected at pages 6-8 of the Office Action as allegedly being unpatentable over Zimmermann in view of Bittner and further in view of Andersson *et al.*, Published International Patent Application No. WO 03/091315 (hereinafter “Andersson”). Applicants respectfully traverse this rejection.

The Office Action suggests that the combined disclosures of Zimmermann and Bittner disclose the claimed invention as set forth above. The Office Action, however, indicates that these references do not disclose that the gelling solution additionally comprises surfactant present in an amount of from 0.05% to .15% by weight; that the solution of the ionically crosslinkable polyionic polymer is kept within a temperature range of 25 to 35°C; or filtering the microspheres through a screen. The Office Action attempts to cure these deficiencies with the disclosure of Andersson, indicating that Andersson discloses the addition of surfactant to a gelling solution, and the use of a temperature of 40°C, and filtering beads through a sieve. The Office Action therefore concludes that the claimed invention would have been obvious. Applicants respectfully disagree with these contentions and conclusions.

As set forth above, Applicants submit that Zimmermann and Bittner, alone or in combination, fail to disclose a process for preparing microspheres using an ultrasonic nebulizer, as recited in the presently claimed invention. Andersson also fails to cure these deficiencies. Thus, Zimmermann, Bittner and Anderson, alone or in combination, do not disclose the presently claimed invention.

In view of the foregoing remarks, Applicants respectfully submit that the Office Action has failed to set forth a proper *prima facie* case of obviousness. Reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a) are respectfully requested.

V. The Rejection of Claim 31 Under 35 U.S.C. § 103(a) Should be Withdrawn

Claim 31 has been rejected at page 8 of the Office Action as allegedly being unpatentable over Zimmermann in view of Bittner and Andersson and further in view of Lemoine *et al.*, *International Journal of Pharmaceutics* 176:9-19 (1998) (hereinafter “Lemoine”). Applicants respectfully traverse this rejection.

The Office Action suggests that the combined disclosures of Zimmermann, Bittner and Andersson disclose the claimed invention as set forth above. The Office Action, however, indicates that these references do not disclose that the surfactant is selected from those compositions set forth in present claim 31. The Office Action attempts to cure these deficiencies with the disclosure of Lemoine, indicating that Lemoine discloses the use of polyoxyethylene sorbitan trioleate as a surfactant in the production of alginate microspheres. The Office Action therefore concludes that the claimed invention would have been obvious. Applicants respectfully disagree with these contentions and conclusions.

As set forth above, Applicants submit that Zimmermann, Bittner and Andersson, alone or in combination, fail to disclose a process for preparing microspheres using an ultrasonic nebulizer, as recited in the presently claimed invention. Lemoine also fails to cure these deficiencies. Thus, Zimmermann, Bittner, Andersson and Lemoine, alone or in combination, do not disclose the presently claimed invention.

In view of the foregoing remarks, Applicants respectfully submit that the Office Action has failed to set forth a proper *prima facie* case of obviousness. Reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a) are respectfully requested.

VI. The Rejection of Claim 33 Under 35 U.S.C. § 103(a) Should be Withdrawn

Claim 33 has been rejected at pages 8-11 of the Office Action as allegedly being unpatentable over Zimmermann in view of Bittner and further in view of Vasington *et al.*, U.S.

Patent No. 5,387,522 (hereinafter "Vasington"), Anderson and Lemoine. Applicants respectfully traverse this rejection.

The Office Action suggests that the combined disclosures of Zimmermann, Bittner, Andersson and Lemoine disclose the claimed invention as set forth above. The Office Action, however, indicates that these references do not disclose that the solution comprises 0.75% to 1.5% by weight of sodium alginate. The Office Action attempts to cure these deficiencies with the disclosure of Vasington, indicating that Vasington discloses the use of low viscosity sodium alginates at about 0.5% to about 1.4%. The Office Action therefore concludes that the claimed invention would have been obvious. Applicants respectfully disagree with these contentions and conclusions.

As set forth above, Applicants submit that Zimmermann, Bittner, Andersson and Lemoine, alone or in combination, fail to disclose a process for preparing microspheres using an ultrasonic nebulizer, as recited in the presently claimed invention. Vasington also fails to cure these deficiencies. Thus, Zimmermann, Bittner, Andersson, Lemoine, and Vasington, alone or in combination, do not disclose the presently claimed invention.

In view of the foregoing remarks, Applicants respectfully submit that the Office Action has failed to set forth a proper *prima facie* case of obviousness. Reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a) are respectfully requested.

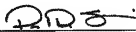
VII. Conclusion

Applicants believe that the claims of the present application are in condition for allowance and respectfully request allowance thereof. The Examiner is invited to telephone the undersigned if that would be helpful in resolving any issues.

With the exception of extension of time fees, no fees are believed due for this submission. The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application or credit any overpayment, to Deposit Account No. 50-5071. Should no proper payment be enclosed herewith, as by the credit card payment instructions in EFS-Web being incorrect or absent, resulting in a rejected or incorrect credit card transaction, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 50-5071.

Respectfully submitted,

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